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Case Report

Natural Malignant Transformation of an Intracranial Epidermoid Cyst

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Malignant transformation of intracranial epidermoid cyst (EC) is very rare, and when it does occur, the clinical course is aggressive. We present an unusual case of natural malignant transformation of an intracranial EC, without a history of surgery. A 61-year-old woman was diagnosed with an EC in the right cerebellopontine angle and prepontine cistern 6 years before the operation described in this report. Her neurological symptoms deteriorated in the 2 months prior to the present admission. Magnetic resonance imaging revealed an irregular, nodular enhanced lesion in the cerebellopontine angle, prepontine cistern, and temporoparietal lobe. Subtotal resection of the lesion was performed. Pathological examination revealed malignant transformation of the EC. The patient died on postoperative day 36 from brainstem infarction, chemical meningitis, and hydrocephalus. Spontaneous rupture of the EC could have contributed to the malignant transformation. This could have been avoided by early removal of the EC.

Key Words: epidermoid cyst, intracranial neoplasms, malignant transformation

Epidermoid cysts (ECs) represent <0.2–1.8% of all intracranial tumors, and are generally regarded as benign intracranial tumors.[1,2] Malignant transformation is very rare, and when it does occur, the course is more aggressive than that of benign ECs.[3,4] We present the case of a 61-year-old woman with natural malignant transformation of an intracranial EC.

Case Report

A 61-year-old woman presented to physicians at Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, China. Six years prior to admission, an EC had been found incidentally (Figure 1), but the patient refused an operation because of concerns regarding

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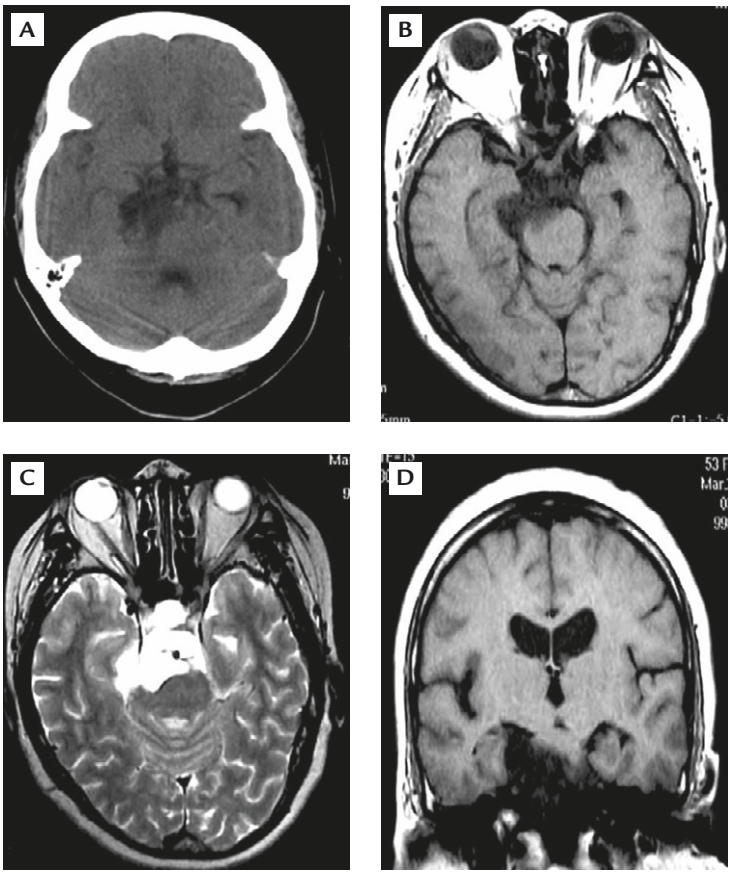

Figure 1. Unenhanced computed tomography and magnetic resonance imaging obtained 6 years before the surgery. (A) Low-density area. (B and D) Slightly long T1 intensity lesion, and (C) a slightly long T2 intensity lesion in the right cerebellopontine angle and prepontine cistern can be seen in the right cerebellopontine angle and prepontine cistern. The brain stem is compressed.

complications. Right facial cranial neuralgia occurred 3 years later, and carbamazepine was used to reduce the pain, followed by radiofrequency treatment. However, 2 months before the current admission, the patient presented with severe headache, nausea, and vomiting. The patient's health deteriorated sharply 1 week before admission. She was found to be lethargic and exhibited poor feeding, with bilateral papilledema. There was decreased touch sensation in the right V2 and V3 distribution and paresis of the 6th cranial nerve. The preoperative Karnofsky performance score was 50.

Magnetic resonance imaging (MRI) of the cranium, with and without gadolinium contrast, revealed an irregular, ring-like enhanced lesion in the right cerebellopontine angle, prepontine cistern, and temporoparietal lobe, with a 3-mm shift of midline structure from right to left, hydrocephalus and brainstem compression (Figure 2). The lesion had clearly increased in comparison with that seen with MRI 6 years previously. Calcification was found by computed tomography (CT). Negative systemic X-ray and ultrasound scanning excluded the possibility of cerebral metastasis from a primary focus located elsewhere in the body.

Using a subtemporal approach, we evacuated some yellowish material of cheese-like consistency and pearly cyst contents; the capsule was hard and adhered tightly to the thalamus and brainstem. The 5th and 6th cranial nerves were involved with the tumor, therefore, the tumor was incompletely removed. Pathological examination of the peri-midbrain part of the tumor revealed squamous cell carcinoma (SCC) and an EC with malignant transformation (Figure 3).

Postoperatively, the patient recovered slightly during the first 3 days but gradually lapsed into a coma due to paresis of the cranial nerves and

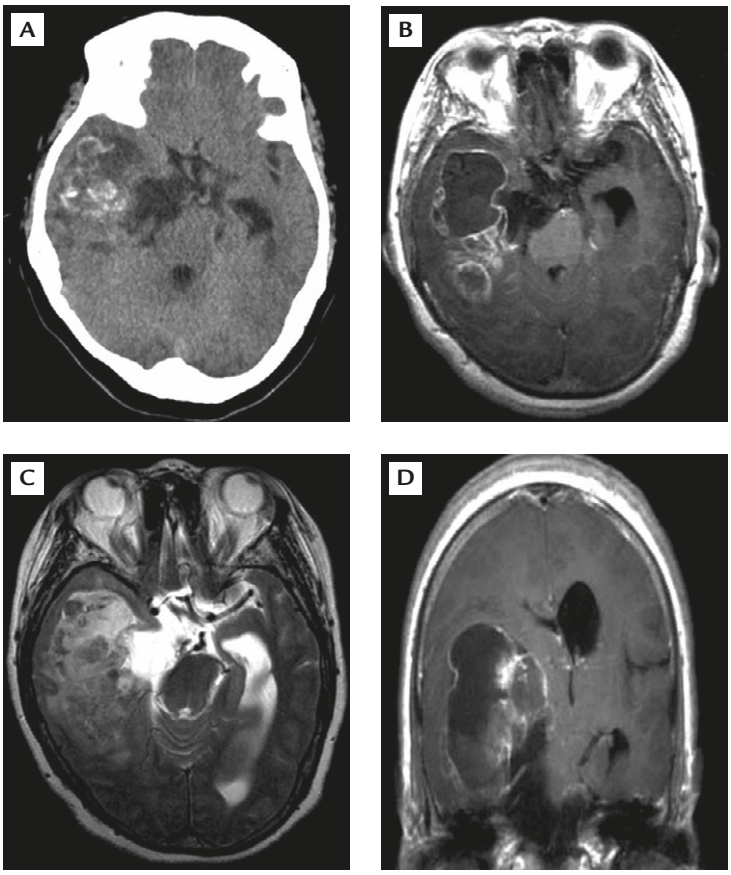

Figure 2. (A) Computed tomography and magnetic resonance imaging showed deteriorated symptoms of patients before surgery, which demonstrated a low-density area in the right cerebellopontine angle and prepontine cistern; an irregular high-density nodular lesion in temporal lobe; and an enlarged ventricle. (B, C, D) Strong enhancement of the wall and irregular nodule in temporal lobe are shown.

brainstem ischemia, which was confirmed by repeated CT (Figure 4). The patient developed refractory fever, in association with aseptic meningitis and pneumonia. Extraventricular drainage and antibiotic treatment did not improve the fever or hydrocephalus. With negative results from the cerebrospinal fluid test and normal temperature 17 days after tumor removal, a ventriculoperitoneal shunt was required for hydrocephalus. This procedure did not lead to the recovery of consciousness. CT revealed progression of the tumor remnant and worsening hydrocephalus. The patient died 36 days after tumor removal.

Discussion

To exclude the possibility of intracranial metastasis of SCC in this patient, systemic examination was necessary, which yielded negative results. Lamellar keratin and squamous epithelium overlapped with irregular atypical cells confirmed malignant transformation of the EC.

Intracranial ECs are generally thought to be benign tumors, and they arise from inclusion of squamous epithelial remnants in the neural tube, when the latter separates from the ectoderm between the 3rd and 5th weeks of embryonic life. Malignant transformation of EC is very rare. Twenty-six cases of malignant transformation of benign ECs have been reported in the English-language literature, including the present case (Table).[1,3,5–22] The 15 male and 11 female patients described in these previous reports ranged in age from 37 to 73 years (mean ± standard deviation, 55.3 ± 9.6 years). The present case is the only malignancy among a total of 577 patients with intracranial EC, who underwent surgery at

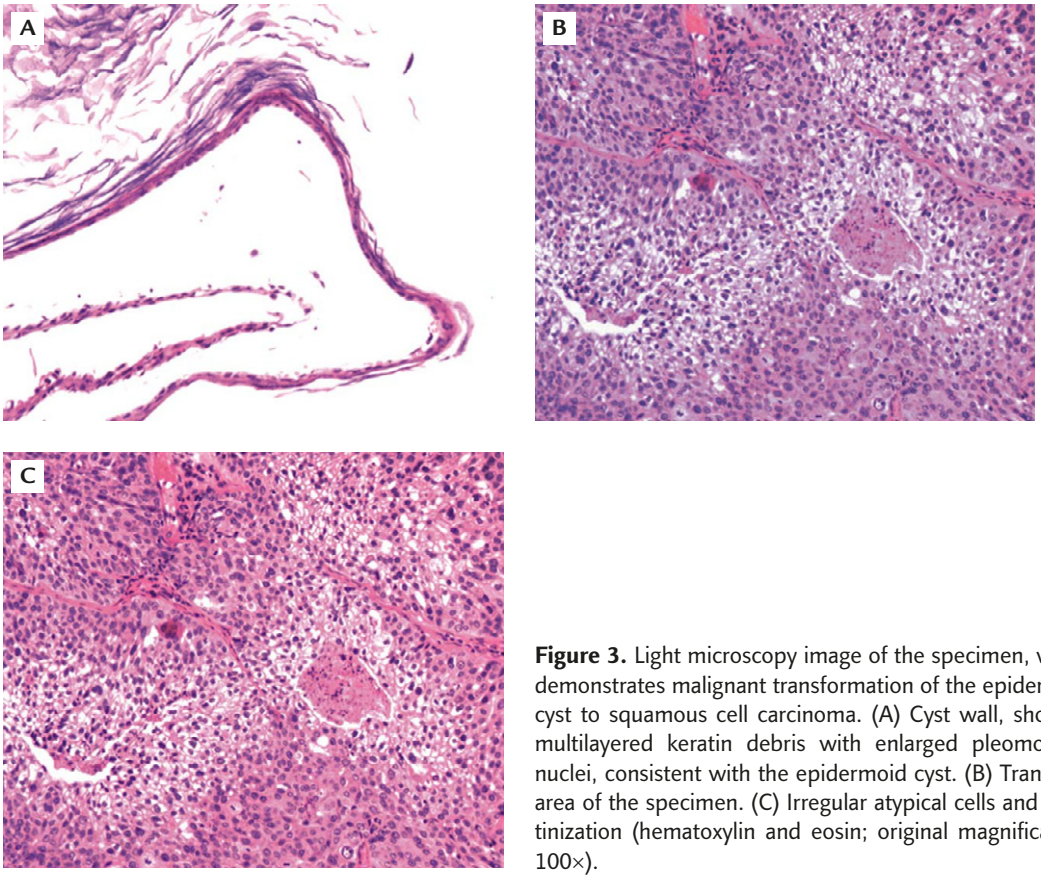

Figure 3. Light microscopy image of the specimen, which demonstrates malignant transformation of the epidermoid cyst to squamous cell carcinoma. (A) Cyst wall, showing multilayered keratin debris with enlarged pleomorphic nuclei, consistent with the epidermoid cyst. (B) Transition area of the specimen. (C) Irregular atypical cells and keratinization (hematoxylin and eosin; original magnification, 100×).

Figure 4. Computed tomography at Day 10 after surgery, which demonstrated enlarged ventricles and a low-density area in the brain stem.

our institution over a 10-year period. The mechanism of this transformation is unclear and no definitive explanation has been provided. It has been suggested that chronic inflammation can predispose patients to malignant transformation.[5] For the present case without a history of previous resection, we hypothesize that spontaneous rupture and leakage of the cyst contents contributed to the malignant transformation.

The symptoms of intracranial SCC vary and are similar to those of EC. However, the clinical characteristics of intracranial SCC include very rapid deterioration with regard to symptoms, and an average duration of 6 months, in contrast to the 47-month duration of a benign EC.[5] The present patient presented with a short history of symptoms of 2 months duration, with rapid deterioration, and development of hydrocephalus.

The growth rate of EC is linear rather than exponential, and abnormal growth indicates malignant transformation.[23] Nishiura et al reported a case of repeated rapid recurrence of cerebellopontine angle EC within 6 months after the first operation, which was diagnosed as epidermoid carcinoma after the third operation.[12] The other CT and MRI features of intracranial SCC are usually irregularly marginated masses that are prominently enhanced in the malignant part of the lesion. In comparison with the initial MRI examination

Table. Primary intracranial squamous cell carcinoma arising in an epidermoid cyst, reported in the English literature.

Case	Report year	Age (yr)/sex	Location	Duration of symptoms	Surgical history*	Interval to SCC	Treatment for SCC	Clinical outcome	Reference
1	1912	52/M	CPA	10 yr	0	–	–	Autopsy	Ernst [5]
2	1960	46/M	Frontal lobe	5 mo	–	–	S	Alive	Davidson & Small [6]
3	1960	73/M	Frontopolar	5 mo	0	–	–	Autopsy	Landers & Danielski [7]
4	1965	50/M	Temporal lobe	8.5 yr	3	7 yr	S	POD, 6 wk	Fox & South [8]
5	1965	54/M	Base of brain	1 yr	2	1 yr	S	POD, 6 wk	Toglia et al [5]
6	1981	53/M	4th Ventricle	4 mo	0	–	S + Rx	POD, 2 mo	Dubois et al [9]
7	1983	53/F	Parasellar	< 12 mo	0	–	S	POD, several wk	Lewis et al [10]
8	1987	56/M	Intra-ventricle	33 yr	1	33 yr	S + Rx	Alive, 3 yr	Goldman & Gandy [11]
9	1989	37/M	CPA	7 yr	1	2 mo	S	–	Abramson et al [5]
10	1989	38/M	CPA	8 mo	2	8 mo	S + Ch	Alive, 2 yr	Nishiura et al [12]
11	1991	67/F	Temporal lobe	> 31 yr	1	31 yr	S	POD, 1 mo	Tognetti et al [13]
12	1993	62/M	Parasellar	2 mo	–	–	S	POD, 1 wk	Acciarri et al [5]
13	1995	58/M	CPA	1 yr	–	–	S + Rx	Alive, 2.5 yr	Nishio et al [14]
14	1999	50/F	CPA	12 yr	1	10 yr	S + Ch + Rx	Alive, 5 yr	Muras et al [15]
15	2001	55/F	CPA	–	1	11 yr	S	POD, 3 mo	Asahi et al [16]
16	2002	57/F	CPA	10 yr	1	2 yr	S	POD, shortly	Link et al [3]
17	2003	65/M	CPA	10 yr	–	–	S + Rx	Alive, 6 mo	Park & Park [5]
18	2003	54/F	Temporal lobe	2 yr	1	3 mo	Ch	Died, 13 mo post-Ch	Hamlat et al [5]
19	2004	45/F	Temporal lobe	12 yr	1	11 yr	S + Rx	Alive, 12 mo	Guan et al [17]
20	2005	45/M	Prepontine	5 wk	0	–	S + Rx	POD, 12 mo	Michael et al [18]
21	2006	56/F	CPA	16 yr	1	8 yr	S + Rx	Alive, 18 mo	Tamura et al [1]
22	2007	65/F	Pineal region	1 mo	0	–	S	Vegetative state	Pagni et al [19]
23	2007	67/M	CPA	8 yr	0	–	Rx	Died, 11 mo post-Rx	Kodama et al [20]
24	2007	45/M	Posterior fossa	1 mo	0	–	S	Lost to follow-up	Agarwal et al [21]
25	2008	72/F	CPA	2 mo	0	–	S + Rx	Alive, 12 mo	Kim et al [22]
26	2008	63/F	Pre-pontine	> 6 yr	0	6 yr	S	POD, 36 d	Present case

**Number of surgery received. M = Male; F = female; CPA = cerebellopontine angle; S = surgery; Rx = radiosurgery; Ch = chemotherapy; POD = post-operative death.*

6 years earlier, we observed clear rapid growth and apparent enhancement of the lesion in the adjacent temporal lobe. These findings strongly suggested malignant transformation.

For benign ECs, it is generally accepted that gross total removal of the tumor can prevent malignant transformation of the remnant. Some ECs involve important brain structures, including the brainstem and/or cranial nerves, which renders complete removal of the tumor impossible. These patients should be followed up for the identification of recurrence and malignant transformation. When transformation to malignancy has occurred, subtotal resection coupled with adjuvant therapy is likely to be the optimal management strategy. Radiosurgery has been used widely to control malignant epidermoid tumors, and the benefits have been well documented.[1,7,15] Patients who have received surgical treatment alone for intracranial SCC have not survived for 3 months. However, the survival time of those who have received postoperative radiotherapy is 21.5 ± 17.4 months.[9,11,13–15,18] Nishio et al reported disease-free survival of > 2.5 years in a patient with primary intracranial SCC after local irradiation.[19] Link et al also reported control of an intracranial SCC for 27 months following stereotactic radiosurgery and external-beam radiotherapy.[3] The effectiveness of chemotherapy remains uncertain in the context of this limited study. As a result of tight adherence of the tumor to the thalamus, brainstem, and cranial nerves in the present case, subtotal resection of the tumor was achieved. Nonetheless, these measures did not prevent brainstem ischemia. Infarction of the brainstem, in combination with the chemical meningitis and hydrocephalus, led to the death of the patient.

Communicating or obstructive hydrocephalus is one of the complications that follow EC removal.[2] In the present case, obstruction of Monro's foramen or overproduction of cerebrospinal fluid may have contributed to communicating hydrocephalus, which could have been responsible for the weak effect of the ventriculoperitoneal shunt.

In summary, we report a case of malignant transformation of an intracranial EC 6 years after radiological diagnosis. The patient's postoperative course was characterized by brainstem infarction and aseptic meningitis, and she died 36 days after surgery. Early removal of the EC could have avoided malignant transformation of the intracranial EC in this patient.

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